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Synthesis of New Ester Linked 1,4-Disubstituted 1,2,3-Bistriazoles and their Antibacterial Evaluation

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Abstract :

A new serial of 1,4-disubstituted 1,2,3-bistriazoles **5a-f** compounds was synthesized via cycloaddition of various bisalkyne **4a-c** with 1-azido-4-nitrobenzene **2a** and 1-azido-4-methylbenzene **2b**. The click reaction the cycloaddition between bisalkynes and the azides carried out in water- tetrahydrofuran (THF) with mixture containing copper sulfate cu (I) as the catalyst and sodium ascorbate as the base. Synthesized 1,4-disubstituted 1,2,3-bistriazoles were characterized by IR, ^{1}H NMR, and ^{13}C NMR techniques. Some of selected compounds were evaluated for antibacterial activity against three bacterial strains:.Gram-positive bacteria *Staphylococcus aureus (S. aureus)* and Gram-negative bacteria *Escherichia coli (E. coli)* and *Acinetobacter baumannii (A. baumannii),* using the disc diffusion method. The results revealed notable antibacterial efficacy. The highest inhibition zone was observed against (*A. baumannii*), likely due to differences in the bacterial cell wall structure.

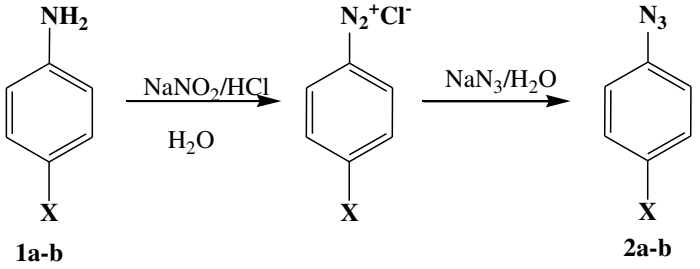
Keywords: Bisalkynes; azides; 1,2,3-bistriazoles; Antibacterial activity

1. Introduction

Triazoles are five-membered heterocyclic compounds that have garnered significant interest from synthetic organic chemists for the development of novel biologically active molecules and medicinal applications. The aromatic composition of triazoles and its electron-rich property donates them to bind with numerous enzymes and receptors by weak interactions like hydrogen bonds, ion-dipole, vander waals force and hydrophobic effect, which enables it to be utilized in several fields. The 1,2,3-triazoles and their derivatives have been documented to possess anti-HIV [1], antimicrobial [2], antiallergic [3], antifungal [4], antitumor [5], selective adrenergic receptor agonist [6], anti-cancer properties [7], anti-convulsant effects [8], antineoplastic [9], and anti-malarial activities [10]. 1,2,3-Triazoles act as essential building blocks in chemistry and exhibit stability against moisture, oxygen, light, and metabolic processes within the body. Considering the pharmacological significance of triazole derivatives, we aimed to synthesize several new 1,4-disubstituted 1,2,3-bistriazoles **5a-f**. Recently, the 1,3-dipolar cycloaddition of azides and terminal alkynes has emerged as the most frequently utilized method for the synthesis of 1,2,3-triazoles. Bisalkyl compounds serve as intermediates in the production of 1,2,3-bistriazoles. To our knowledge, all the compounds we have synthesized are novel. The bisalkynes **4a-c** were produced by reacting acid dichloride **3a-c** with propargyl alcohol in the presence of triethylamine (TEA) in chlorofor ($CHCL_3$), adhering to the literature procedure [11]. The click reaction between bisalkynes **4a-c** and azides **2a-b** was conducted in a water-THF mixture with copper sulfate as the catalyst and sodium ascorbate as the base, resulting in the desired products **5a-f** with good yields of 72-95%. Furthermore, the antibacterial evaluation of selected compounds is included.

2. Results

The 1,2,3-bistriazoles **5a-f** were prepared according to known procedure from various bisakynes **4a-c** and azides **2a- b [11**]. A significant role for organic azides has emerged at the nexus of materials science, biology, medicine, and chemistry**.** We prepared the starting material, aromatic azides **٢a-b**, which was easily synthesized in high yield (92 and 84%) respectively, it was prepared by an on-pot reaction by diazotization of aromatic amines **1a-b** (p-nitro aniline and p-methyl aniline) by dropwise addition of HCl (concentrated) and aqueous sodium nitrite followed by reaction with sodium azide while maintaining the temperature below (-5°C); because the reaction is exothermic due to the formation of unstable diazanium salts at room temperatures (Scheme 1).



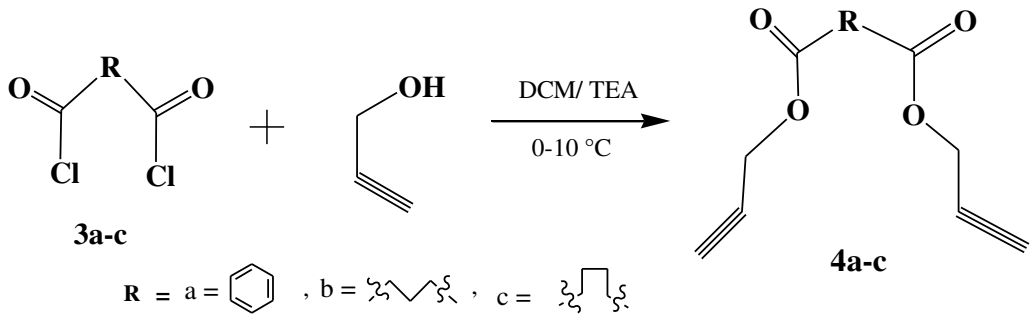
1a-b **2a-b**

1a, X= NO_2. 1**b,** X= CH_3

Scheme 1

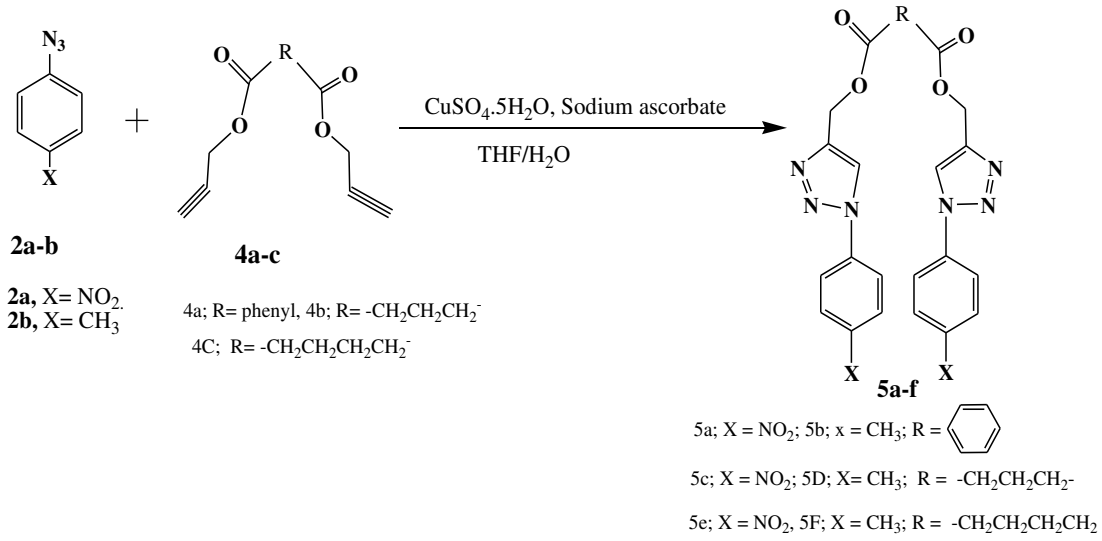
propogyl alcohol have served as significant starting materials in the synthesis of various heterocyclic compounds, including triazole. The propargyl group is recognized as a versatile functional group utilized in the fields of chemical, pharmaceutical, and material chemistry. The bisalkynes **4a-c** were obtained by treating each of the acid dichlorides **3a-c** (isophthaloyl dichloride, glutamyl dichloride, and adipoyl dichloride) (4.03 mmol) with propargyl alcohol (470 µl, 8.03 mmol). These were then suspended in a mixture of

CH_3Cl (25 mL) and triethylamine (2.2 mmol) while kept on ice, following the procedure outlined in the literature [11], as illustrated in Scheme 2.



Scheme 2

The reaction between azides **2a-b** (2.2 mmol) and bisalkynes **4a-c** (1mmol) under nitrogen gas atmosphere were suspended in a 1:1 mixture of water and tetrahydrofuran THF(3 ml of each). To this reaction, sodium ascorbate (0.2 mmol) and Cupric sulfate pentahydrate $CuSO_4.5H_2O$ (0.1 mmol) were added to the mixture. The reaction mixture was stirred overnight. Upon completion of the reaction, the reaction mixture was diluted with cold water and extracted with ethyl acetate. The combined organic layer was dried over anhydrous Sodium sulfate Na_2SO_4 filtered and concentrated under vacuum to yield 1, 4-disubstituted 1, 2, 3-bistriazoles **5a-f** in good to excellent yields, 80-99%.



Scheme 3

All the synthesized 1,2,3-bistriazoles were well characterized by IR, ^{1}H NMR, and ^{13}C NMR spectroscopy. In the IR spectra, the formation of 1,2,3-bistriazoles was apparent from the absorption band in the region 3156-3090 cm^{-1} due to =C–H (stretching) of triazole ring. In addition, the C-H aliphatic stretching vibrations bands are observed v = 2934-2970 cm^{-1}. The carbonyl group C=O and N=N aromatic stretching vibrations bands are observed between v = 1698 - 1741 and 1540-1671 cm^{-1}, respectively. In ^{1}H NMR the characteristic singlet signal appearance in the region of δ 8.23-8.79 ppm due to the vinylic protons CH=C of triazole ring. While, the characteristic singlet signal in ^{13}C NMR appearance in the region of δ 143.2-144.3 ppm due to carbon (CH=C) of the triazole ring. In addition, the signals appeared at δ = 120.4-121.3 ppm are assignable to carbon 2C-CH-N of triazole ring showed the formation of triazole ring.

3. DISCUSSION

Based on recent studies on 1,4-disubstituted 1,2,3-triazoles, will submit show provide comparisons between the results of my studies and those found in the literature. In a study published in Chemical Biology Letters, various 1,4-disubstituted triazoles were synthesized and analyzed using FT-IR and NMR spectroscopy, showing similar IR absorption bands in the range of 3000–3100 cm^{-1} for CH stretches and around 1600 cm^{-1} for C=N stretch, which is consistent with the bands observed in this studies. Specifically, the ^{1}H-NMR spectra for these compounds showed typical triazole proton signals between 7.5–8.5 ppm, which aligns with the proton shifts in this reported for synthesized compounds.[12] Moreover, in another study focusing on triazole derivatives for antimicrobial activity, IR and NMR analysis revealed key characteristic peaks in the C-H stretch around 2930 cm^{-1} and N-H bending around 1550 cm^{-1}. These findings also support IR and NMR observations in this sdudies, confirming the consistency of results with the broader trends seen in these recently synthesized triazole derivatives.[13]

The IR analysis of 1,4-disubstituted 1,2,3-triazoles **5a-f** shows characteristic absorption bands for various functional groups. data for the C-H (aliphatic) stretch at 2934-2970 cm^{-1} is in line with findings from recent studies that report C-H stretching in the range of 2850–2960 cm^{-1} for aliphatic groups in similar triazole derivatives. This shift might be influenced by the specific substitutions on triazole rings, which can modify the stretching frequency. The C=O stretch observed between 1698–1741 cm^{-1} in synthesized compounds correlates closely with values reported in the literature [13], where C=O stretches in triazole derivatives appear around 1710–1740 cm^{-1}. This suggests a consistent presence of carbonyl groups in synthesized compounds, similar to those found in recent triazole-based studies. For the N-H and N=N stretches associated with the triazole ring, found recorded range of 1555–1672 cm^{-1} aligns well with other recent work, where N-H bending and N=N stretching have been reported between 1540–1650

cm^{-1}. These findings support the typical triazole structure in synthesized compounds, confirming that the characteristic heterocyclic features are maintained. In terms of ^{1}H-NMR, showed observed shifts for aromatic protons around 7.5–8.0 ppm are consistent with the proton chemical shifts reported for 1,2,3-triazole derivatives in the literature. Similarly, the aliphatic proton signals in synthesized compounds, appearing between 1.5–2.5 ppm, are in good agreement with reported values for similar structures. ^{13}C-NMR results for carbonyl carbons around 165–172 ppm and aromatic carbons in the 120–144 ppm range are also in line with previous reports, further confirming the structural integrity of synthesized compounds. Both studies suggest that the spectral data is reported is in line with current research on triazole derivatives, particularly with respect to their aromatic and triazole ring environments. This comparison help validate this findings and demonstrate the relevance of synthesized compounds within the broader scope of triazole research.

3. Antibacterial evaluation

The antibacterial activity of all new synthesized compounds was evaluated using the agar diffusion technique [١4]. The compounds were prepared and tested at ٥٠ mg/ml concentration in dimethylsulfoxide (DMSO). The tested organisms were both Gram-negative bacteria *(E. coli* and *A. baumannii*) and Gram-positive bacteria *(S. aureus)*. The bacteria were maintained in nutrient agar and Mueller Hinton agar media, respectively. After 24 h incubation at 37°C, the diameter (mm) of the inhibition zones was measured. DMSO showed no inhibition zones. Streptomycin (ST) in a concentration of 10 mg was used as reference for antibacterial activities. The antibacterial activities of all synthesized compounds are listed in Table 1. According to the results calculating the average repeat for each compound separately, we found that the synthesized 1,4-disubstituted 1,2,3-bistriazoles compounds demonstrated significant

antibacterial activity against (E. coli, A. baumannii, and S. aureus). The most notable activity was observed against (A. baumannii), with inhibition zones exceeding those for the other two bacteria. The compounds **5a, 5c-d, 5f** were effective against all tested bacterial strains. Although, compound **5f** have inhibition effect on (E. coli, S. aureus and A. baumannii), but it observed that it has lower inhibition power compared to compounds compound **5a, 5c-d**. Compound **5b** was active against all tested bacterial strains except (S. aureus). In opposite to, Compound **5e** was active against all tested bacterial strains except Escherichia coli. The synthesized 1,4-disubstituted 1,2,3-bistriazoles compounds demonstrated significant antibacterial activity against *(E. coli, A. baumannii),* and *(S. aureus).* The most notable activity was observed against *(A. baumannii)*, with inhibition zones exceeding those for the other two bacteria. These findings align with prior research but also highlight some distinctions that merit further exploration. Compared the effect of the compounds on the three types of bacteria, and it was noted that the least effect eas on *(E.coli)* and stronger effect on *(A. baumannii)* inhibition zones of up to 20 mm and 15 mm against *(S. aureus)*. A study by Strzelczyk *et al.,* (2021)[15] evaluated 1,2,4-triazole derivatives and reported inhibition zones of up to 20 mm against *(S. aureus)* and approximately 15 mm against *(E. coli).* This difference in activity may be due to variations in the chemical substitutions on the triazole rings, which can alter interactions with bacterial cell walls**.** The differences between this study and prior findings can be attributed to their Chemical Structure. The presence of specific substituents in the synthesized compounds may enhance their affinity for bacterial targets, particularly in *(A. baumannii),* experimental Conditions: Variations in compound concentration, solvent choice, and bacterial growth media could influence the observed activity. In another recent study by El Hassani *et al.* (2024) [16], derivatives synthesized via microwave-assisted techniques showed enhanced efficacy against *(A. baumannii)*. The superior activity was attributed to the unique structural modifications in these compounds, particularly the incorporation of electron-withdrawing groups that

improve lipophilicity and cellular penetration. Compound 1,4-disubstituted 1,2,3 bistriazoles (**5c**) exhibited significant antibacterial activity against all tested bacterial strains.

Table 1. Antibacterial activities (conc.50 mg/ml) of 1, 4- substituted 1, 2, 3 bistriazoles **5a-f .**

Compound No. (50 mg/ml)	**Zone of Inhibition(mm)**		
	Gram-negative bacteria		Gram-positive bacteria
	E. coli	***A. baumannii***	***S. aureus***
°a	9	23	15
°b	10	25	-
°c	11	25	15
5d	15	23	15
5e	-	25	12
5f	10	22	11

4. Experimental Section

4.1 Instrumentation

All melting points were determined using a hot-stage Gallenkamp melting point apparatus. Infrared spectra IR were recorded using a Shimadzu DR-8001 spectrophotometer as KBr pellets. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker, at 400 MHz and 100 MHz in DMSO-d_6 as a solvent with tetramethyl silane (TMS) as internal standard; chemical shifts are reported in δ (ppm). General-purpose to use thin layer chromatography (TLC) with Ultraviolet (UV) indicators in experiments to monitor the completion of reactions. Column chromatography was performed using silica gel Merck No. 5545 in ethyl acetate**:** n-hexane (2:3) as eluent to purification azide compounds while using ethanol: Dimethyl formamide (DMF) (1**:**1) to purification bisalkynes compounds and also purification of bistriazoles compounds by Column chromatography or using ethanol**:** dimethyl sulfoxide DMSO (1**:**1).

4.2 General Method to Synthesis of Starting Materials Azides 2a-b.

The starting material was prepared according to the method described by Li *et al*. in (2007) [17], as follow: A solution of concentrated hydrochloric acid (6 N, 19.5 ml) and (11 ml, 15 mmol) of each of the required aryl amine **2a-b** (p-nitro aniline and p-methyl aniline) in water was added and cooled to (0 °C) string for 5 min. A solution of sodium nitrite (15 mmol) in water (11 ml) was then added dropwise to the reaction mixture while maintaining the temperature below (-5 °C). The reaction mixture was stirred for 1h. A solution of sodium azide (16.5 mmol) in water (11 ml) was then added dropwise to the reaction mixture while maintaining the temperature below (-5 °C). The reaction mixture was warmed to room temperature and stirred overnight. The progress of the

reaction was monitored by TLC. The organic layer was separated, and the aqueous layer was extracted with dichloromethane CH_2Cl_2 DCM (3 × 20 ml). The combined organic layers were washed with an aqueous solution of bicarbonate sodium $NaHCO_3$, then brined, dried sodium sulfate Na_2SO_4 and filtered. Then, evaporation of the solvent *in vacuo* gave the crude azides **2a-b** and purification by column chromatography using ethyl acetate: n-hexane (2: 3) as eluent.

a. ١-Azido-4-nitrobenzene 2a.

Yield, (92%); yellow solid; m.p = 72-73°C; FT-IR (KBr, cm^{-1}) *v*: 3090 (CH=, Ar), 2100 (N≡N).

b. ١-Azido-4-methylbenzene 2b.

Yield (84%); brown oil; FT -IR (KBr, cm^{-1}) *v*: 3030 (CH=, Ar), 2923-2983 (C-H, Aliphatic), 2101 (N≡N).

3.4 General Method Synthesis of Bisalkynes 4a-c.

The starting material bisalkynes **4a-c** was prepared according to the method described by Haridas *et al.* in (2011) [18] as follows: propogyl alcohol (470 µl, 8.03 mmol) and each of acid dichloride **3a-c** (4.03 mmol) were suspended added to a mixture of Chloroform CH_3Cl (25 mL) and triethylamine (2.2 mmol) in ice cold. The reaction mixture was stirred overnight. Upon completion of the reaction, the mixture was concentrated under a vacuum to yield bisalkynes **4a-c**, which were purified by ethanol and DMF (1:1).

a. Diprop-2-ynyl isophthalate 4a.

Yield, (95%); white solid; m.p = 84-85 °C; FT-IR (KBr, cm^{-1}) *v*: 2841 (CH–aliphatic), 2130 (C≡C), 1724, 1708 (C=O); ^{1}H NMR (600 MHz, DMSO-d_6) *δ*: 8.45 (s, 1H, CH=, Ar), 8.20 (d, 2H, 2CH=, Ar), 7.71 (t, 1H, CH=, Ar), 4.99 (s, 4H, $2CH_2$–O), 3.63 (s, 2H, 2CH≡); ^{13}C NMR (150 MHz, DMSO-d_6) *δ*: 164.6 (2C=O), 134.6 (2CH=C-, Ar), 130.3 (2CH-C=CO, Ar), 130.1 (CH-C-C=O, Ar), 130.0 (CH=CH=CH, Ar), 78.7 (2C≡CH), 78.6 (2C≡CH), 53.5 ($2CH_2$–O).

b. Diprop-2-ynyl glutarate 4b.

Yield, (88%); brown liquid; FT-IR (KBr, cm^{-1}) *v*: 2949 (CH-aliphatic), 2130 (C≡C), 1733, 1740 (C=O); ^{1}H NMR (600 MHz, DMSO-d_6) *δ*: 4.60 (s, 4H, $2CH_2$–O), 2.46 (s, 2H, 2CH≡), 2.36 (t, 4H, $2CH_2$–CO), 1.90 (m, 2H, CH_2–CH_2–CH_2); ^{13}C NMR (150 MHz, DMSO-*d6*) *δ*: 171.9 (2C=O), 77.6 (2C≡CH), 75.1 (2C≡CH), 32.7 (CH_2–CH_2–CH_2), 19.7 (CH_2–CH_2–CH_2), 51.9 ($2CH_2$–O).

c. Diprop- 2-ynyl adipate 4c.

Yield, (86%); white solid m.p =105-106 °C FT-IR (KBr, cm^{-1}) *v*: 2874, 2947 (CH-aliphatic), 2129 (C≡C), 1749, 1740 (C=O); ^{1}H NMR (600 MHz, DMSO-d_6) *δ*: 4.59 (s, 4H, $2CH_2$–O), 2.46 (s, 2H, 2CH≡), 2.31 (t, 4H, $2CH_2$–CO), 1.60 (t, 4H, $2CH_2$); ^{13}C NMR (150 MHz, CD_3CL) *δ*: 171.2 (2C=O), 77.7 (2C≡CH), 75.0 (2C≡CH), 51.8 ($2CH_2$–O), 33.4 ($2CH_2$–C=O), 24.0 ($2CH_2$).

3.5 General procedure for synthesizing 1, 4-disubstituted 1, 2, 3 bistriazoles 5a-f.

Azides **2a-b** (2.2 mmol) and from each of bisalkynes **4a-c** (1 mmol) under nitrogen atmosphere were suspended in a 1:1 mixture of water and tetrahydrofuran THF (3 ml each). To this reaction, sodium ascorbate (0.2 mmol) and Cupric sulfate pentahydrate $CuSO_4.5H_2O$ (0.1 mmol) were added to the mixture. The reaction mixture was stirred overnight. Upon completion of the reaction, the reaction mixture was diluted with cold water (20 ml) and extracted with ethyl acetate (10 x 2 ml). The combined organic layer was dried over anhydrous Sodium sulfate Na_2S0_4 filtered and concentrated under vacuum to yield 1, 4-disubstituted 1, 2, 3-bitriazoles **5a-f**, which were purified by Ethanol: DMSO (1:1) **[11].**

3.5.1. Synthesis of bis ((1-(4-nitro phenyl)-1*H*-1, 2, 3- triazole- 4 yl) methyl) isophthalate 5a.

Yield, (95%); orange crystal; m.p = 210-211 ^oC; IR (KBr, cm^{-1})ν; 3575 (OH, enol), 3117 (=CH, triazole), 3091 (=CH, Ar), 2970 (CH, aliphatic), 1698 (C=O), 1611 (N=N); ^1H NMR (600 MHZ, DMSO-d_6) δ (ppm):, 9.15 (s, H, CH=, Ar), 8.54 (s, 4H, 4CH=, Ar), 8.43 (d, 4CH=), 8.27 (d, 4H, 4CH=, Ar), 7.73 (t, 4H, 4CH=, Ar), 5..58 (s, 4H,2CH_2-O); ^{13}C NMR (DMSO-d_6) δ (ppm): 165.0 (C=O), 147.3 (2C-NO_2, Ar), 144.0 (C=CH, triazole), 141.2 (2=C-N), 134.5 (2 CH=, Ar), 130.5 (2=C-C=O, Ar), 130.3 (CH=, Ar), 130.1 (CH=CH-CH, Ar), 125.9 (4CH=C-NO_2, Ar), 124.0 (4CH=C-, Ar), 121.3 (2=CH-N, triazole), 58.5 (2CH_2-O),

3.5.2. Synthesis of bis ((1-(4-tolyl)-1*H*-1, 2, 3- triazol- 4yl) methyl) isophthalate 5b.

Yiled, (82%); white crystal; m.p = 262-263 ^oC ; IR (KBr, cm^{-1})ν: 3422(OH, enol), 3132 (=CH, triazole), 3090 (CH, Ar), 2969 (CH,aliphatic), 1715 (C=O), 1520 (N=N);

^{1}HNMR (DMSO-d_6) δ (ppm):8.89 (s, CH=, Ar), 8.53 (d, 2H, 2CH=, Ar), 8.28 (2H, 2CH=, triazole), 7.80 (t, H, CH=, Ar), 7.74 (d, 4H, 4CH, Ar), 7.41 (d, 4H, 4CH=, Ar), 5.54 (s,4H, 2CH-O), 2.39 (s, 6H, 2CH_3, Alipha); ^{13}C NMR (DMSO- d_6) δ (ppm): 21.0 (-CH_3, Alipha), 165.1(C=O), 143.2 (2C=CH, triazole), 138.9 (2-C-CH_3, Ar) , 134.8 (4CH=C-N, Ar), 134.4(2CH=CH, Ar), 130.6 (2=C-N, Ar), 130.5 (2C-C=O, Ar), 130.2 (CH-C-C=O, Ar), 130.1 (4CH=C-CH_3, Ar), 123.4 (CH=, Ar), 120.6 (2=C-N, triazole), 58.6 (2CH_2-O).

3.5.3. Synthesis of bis ((1-(4-nitrophenyl)-1*H*-1 ,2, 3-triazol-4 yl) methyl) glutarate 95c.

Yield, (81%); orange crystal m.p = 159 ^{o}C; IR (KBr) (cm^{1}) ν: 3127(=C-triazole), 3093 (=CH, Ar), 2966 (CH, Aliph), 1733 (C=O), 1527 (N=N); ^{1}HNMR (DMSO-d_6), δ (ppm): 9.03 (d, 4H, 4CH-C-NO_2, Ar), 8.43 (d, 4CH=, Ar), 8.23 (s, 2H, 2CH=, triazole), 5.27 (s, 4H, 2CH_2-O), 2.44 (t, 4H, 2CH_2-C=O, Aliph), 1.85 (m, 2H, CH_2, Aliph), , C^{13}NMR (DMSO-d_6), δ (ppm): 172.5 (2C=O), 147.3 (2CH-C-NO_2), 144.2 (2 =CH-C-CH_2, triazole), 141.2 (2N-C, Ar), 125.9 (4CH-C-NO_2, Ar), 123.7 (4CH-C-N, Ar),), 121.2 (2C-CH-N, triazole), 57.3(2CH_2-O), 32.9 (2CH_2-C=O, Aliph.), 20.2 (CH_2-CH_2-C=O, Aliph).

3.5.4. Synthesis of bis ((1-(p-tolyl) -1*H*-1, 2, 3-triazol-4 yl) methyl) glutarate 5d.

Yield, (72%); dark brown; m.p = 210-212; IR(KBr, cm^{-1}) ν; 3140 (=CH-triazole), 3099 (=CH, Ar), 2961 (CH, Aliph.), 1718 (C=O),1560 (N=N); ^{1}HNMR (DMSO-d_6), δ (ppm): 8.79 (s, 2CH=, triazole), 7.78 (d, 4H, 4CH, Ar), 7.39 (d, 4H, 2CH_2-C-CH_3, Ar), 5.23 (s, 4H, 2CH_2-O), , 2.44 (t, 4H, 2CH_2-C=O, Aliph.), 2.40 (s, 6H, 2CH_3), 1.82 (m, 2H, CH_2, Aliph) ^{13}C NMR (DMSO-d_6), δ (ppm) : 172.6(2C=O), 143.4 (2=CH-C-CH_2, triazole), 138.8 (2CH-C-CH_3, Ar), 134.7 (4CH-C-N, Ar), 130.6 (2N-C, Ar), 123.2

(4CH-C-CH_3, Ar), 57.4 ($2CH_2$-O), 32.8 ($2CH_2$-C=O, Aliph), 21.0 ($2CH_3$, Aliph), 20.21 (CH_2-CH_2-C=O, Aliph).

3.5.5. Synthesis of bis ((1-(4-nitro phenyl)- 1*H*-1, 2, 3- triazol-4 yl) methyl) adipate 5e.

Yield, (79%); yellow crystal; m. p = 200 ^oC; IR (KBr, cm^{-1}); 3128 (=CH, triazole), 3093 (CH-Ar), 2934 (CH-aliph), 1725 (C=O), 1596 (N=N); ^1H NMR (DMSO-d_6), δ (ppm): 9.02 (d, 4H, 4CH-C-NO_2, Ar), 8.45 (d, 4H, 4CH, Ar), 8.23 (s, 4H, 4CH-Ar), 5.25 (s, 4H, $2CH_2$-O), 2.39 (t, 4H, $2CH_2$-C=O, Aliph), 1.59 (m, 4H, $2CH_2$, Aliph), ^{13}C NMR (DMSO-d_6), δ (ppm): 172.8 (2C=O), 147.3 (2CH-C--NO_2, Ar), 144.3 (2CH=C-CH_2, trizole), 141.2 (2N-C, Ar), 24.2 ($2CH_2$), 125.9 (4CH-C-NO_2), 123.6 (4CH-C-N, Ar), 121.2 (2C-CH-N, trizole),), 33.4 ($2CH_2$-C=O, Aliph), 24.2 (CH_2-CH_2-C=O, Aliph).

3.5.6. Synthesis of bis ((1-(p-tolyl)- 1*H*-1, 2, 3- triazol-4 yl) methyl) adipate 5f.

Yield, (57%) sandy crystal m. p = 116 ^oC; IR (KBr, cm^{-1}): 3135 (=CH, triazole), 3093 (CH-Ar), 2953 (CH-Aliph), 1929 (C=O), 1559 (N=N); ^1H NMR (DMSO-d_6), δ (ppm) : 8.78 (s, 2H, 2CH=, triazole), 7.78 (d, 4H, 4CH, Ar), 7.39 (d, 4H, 4CH-C-CH_3, Ar), 5.22 (s, 4H, $2CH_2$-O), 2.51 (t, 4H, $2CH_2$-C=O, Aliph), 1.57 (m, 4H, $2CH_2$, Aliph), ^{13}C NMR (DMSO-d_6), δ (ppm): 172.9 (2C=O), 143.5 (2=CH-C-CH_2, triazole), 138.8 (2CH-C-CH_3, Ar), 134.7(4CH-C-N, Ar), 130.6 (2N-C, Ar), 123.1 (4CH-C-CH_3, Ar), 120.4 (2C-CH-N, trizole), 57.3 ($2CH_2$-O), 33.4 ($2CH_2$-C=O, Aliph), 24.2 (-CH_2-CH_2-C=O, Aliph), 21.0 ($2CH_3$).

5. Conclusions

In conclusion, synthesis of some ester linked 1,4-disubstituted 1,2,3-bistriazoles have been reported by Cu catalysed azide-al- kyne cycloaddition using different aliphatic and aromatic moieties. The antimicrobial activity studies revealed that the compounds screened showed moderate to good activities, fitness of most active all compounds against *(A. baumannii)*. This study focuses on the use of organic synthesis to prepare some ester linked 1,4-disubstituted 1,2,3-bistriazoles compounds through three distinct reaction stages. In the first stage, aromatic azides 2a-b were synthesized by reacting aromatic amines **2a-b** with sodium azide, leading to a variety of aromatic compounds containing the azide group. In the second stage, bisalkynes **4a-c** was synthesized by reacting acid dichlorides **3a-c** with propargyl alcohol, resulting in successful formation of bisalkynes compounds. In the third stage, 1,4-disubstituted 1,2,3-bistriazoles were synthesized by reacting the aromatic azides with bisalkynes. The resulting compounds were analyzed using various spectroscopic techniques such as FT-IR, ^{1}H NMR and ^{13}C NMR to confirm their chemical structure. The analytical data showed that the synthesized compounds matched the expected structures. Regarding the antibacterial study, the antibacterial activity of these compounds was tested against three bacterial strains: Gram-positive bacteria (*S. aureus*) and Gram-negative bacteria (*A. baumannii* and *E.coli)*. The compounds **5a-f,** showed significant inhibition of bacterial growth, with the strongest effect observed against *A. baumannii* , followed by *S. aureus* , and the least effect against *E.coli*. This suggests that these compounds have potential as antimicrobial agents, enhancing their pharmaceutical applications as antibiotics against certain bacterial strains. The findings of this research are consistent with previous studies, emphasizing the antibacterial potential of bis-triazole derivatives. However, the superior activity against *A. baumannii* in this study provides new insights into the role of structural modifications in enhancing efficacy. Future studies should focus on

elucidating the exact mechanisms of action and optimizing these compounds for clinical use.

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